REMARKS/ARGUMENTS

In view of the foregoing amendments and following remarks, favorable reconsideration of the pending claims is respectfully requested.

Status of the Claims

Claims 2 and 4-10 are pending. Claims 1 and 3 have been cancelled. By way of this amendment, Claim 10 is cancelled.

Claim 1 has been amended to recite that the method comprises the step of administering the recited alkanols and to clarify that the active ingredient consists of the recited alkanols and that additional components, such as a carrier, are not excluded.

Claim Objections

Claim 7 has been objected as assertedly being of improper dependent form. It is respectfully submitted that the amendment to Claim 7 has rendered this objection moot.

The Examiner has also objected to Claim 10. Claim 10 has been cancelled and therefore this objection is moot as well.

Prior Art Rejections

Claims 2 and 4-10 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Vail, III (US 7,150,881) as evidenced by Swords et al. (Composition of Australian Tea Tree Oil (Melaleuca alternifolia); or in the alternative, under 35 U.S.C. § 103(a) as being obvious over the combination of Vail and Swords.

Vail relates to methods and apparatus for the inhalation of eucalyptus oil and tea tree oil vapors so as to prevent and/or treat opportunistic infections of the human respiratory system, including those caused by pathogens such as the common cold, influenza and tuberculosis. Eucalyptus oil and tea tree oil are naturally occurring products isolated from the eucalyptus and tea tree trees respectively, which grow in the wild in mainland Australia and recently have begun to be cultivated so that these products can be more easily harvested. In particular Vail relates to the periodic inhalation of vapors from combinations of these products which occur either spontaneously or which are generated using an apparatus they have developed. Vail does not disclose any sort of dosage regime, such as a quantity of vapor to be inhaled per dosage.

The combination of Vail and Swords does not disclose or suggest the claimed invention. In order for a claim to be anticipated or rendered obvious by a reference or combination of

references, each and every element must be disclosed or suggested by the reference or combination of references. In the present case, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obvious, because Vail, whether considered individually or in combination with Swords, does not disclose each and every element of the claimed invention.

First, Vail does not disclose or suggest a method of partially or fully activating cystic fibrosis transmembrane conductance regulator channels (CFTR) in epithelial cell membranes. In fact, Vail relates to a different technical problem than the claimed invention. The claimed invention is directed to the activation of defective CFTRs, Vail does not claim or show that eucalyptus oil or tea tree oil, or any of the various components thereof, have any effect upon defective CFTRs. The section of Vail to which the examiner refers (column 28 line 31 to column 31 line 31) does not concern the activation of CFTRs, but instead concerns a symptom of Cystic Fibrosis namely the occurrence of opportunistic infections resulting from the production of overly thick mucus and the belief of the inventors in Vail, unsupported by any sort of experimental evidence, that the inhalation of eucalyptus oil and tea tree oil vapors could prevent, treat or at least minimise the effects of these infections.

It is not possible therefore starting from Vail to arrive at the method according to clam 9 which concerns the administration of at least one C_6-C_{10} alcohol to patients with defective CFTRs so as to partially or fully activate these in cells exposed to the alcohol.

As noted above, amended Claim 9 relates exclusively to a method wherein only an active ingredient consisting of at least one C_6-C_{10} alcohol, is administered to patients with defective CFTRs. The administration of tea tree oil which comprises a complex mixture of several mainly phenyl group containing organic compounds, to the lungs of a patient with defective CFTRs does not disclose or suggest the claimed method.

Further, the combination of Vail and Swords does not disclose or suggest a method that includes administering a<u>CFTR activating agent consisting of</u> at least one linear n-alkanol selected from the group consisting of C_6-C_{10} as recited in Claim 9. The examiner alleges that Swords Tea Tree oil comprises a trace quantity (based upon combined gas-chromatography/mass spectrometry) of hexanol and that therefore if Tea Tree oil were to be administered to the lungs of a patient with defective CFTRs and that this would activate these defective CFTRs. Based

upon the Examiner's reasoning therefore, a patient with cystic fibrosis, i.e. one with a vastly reduced lung capacity, would inhale along with the trace amount of hexanol all the other components of Tea Tree Oil, which include several Phenyl containing compounds which as well as being highly aromatic are also caustic. The caustic nature of these compounds being the reason why they have generalized antibiotic effects which in turn is the reason why Vail uses Tea Tree Oil to prevent and/or treat opportunistic infections of the human respiratory tract.

According to the Examiner's calculation Tea Tree Oil may contain as much as 0.004% of hexanol (v/v) which is within the scope of concentrations considered appropriate by the inventors in the present Patent Application 0.001% to 0.01% (v/v) to be present in the solution administered to the Patient, but the examiners suggestion that a solution of up to 99% Tea Tree oil (and 1% Eucalyptus Oil) as per Vail could be vaporized and inhaled so as to generate in the vicinity of the epithelial cells of the patient a concentration of hexanol sufficient to activate (partially or fully) the CFTR is absurd. What the Examiner suggests is different to the teaching of Vail in a very important and specific way, Vail concerns exposing the respiratory tract to the vapor of Tea Tree Oil (plus that of Eucalyptus Oil) so as to provide an additional level of innate immunity to combat air borne pathogens. The quantity of Tea Tree Oil inhaled to achieve this effect although not specified in Vail must be a miniscule amount so as to prevent damage to the lungs by the various caustic compounds present in Tea Tree Oil.

The inventors have established that it is necessary to achieve a certain concentration of the C_6-C_{10} alcohol around the target cell/defective CFTR, see figure 2 of the present Patent Application. In particular the inventors have found that a concentration of 1mM (of Octanol) or more achieves optimal levels of CFTR activation. As such, the combination of Vail and Swords also does not teach a method that includes the step of administering to said patient a CFTR activating agent consisting of at least one linear n-alkanol selected from the group consisting of C_6-C_{10} in an amount sufficient to generate in the vicinity of said epithelial cell membranes a concentration of said n-alkanol sufficient to partially or fully open said CFTR in said epithelial cell membranes.

Based upon the teaching of Swords' and the Examiner's estimation of the concentration of hexanol in Tea Tree Oil, in order for hexanol to be administered so as to achieve a concentration of 1mM hexanol in a portion of the Patients lungs (equivalent to 1 litre of water), 0.10217g of hexanol would need to be present (MW Hexanol = 102.17 therefore 1M =102.17g/l), the total amount of tea tree oil which would need to be in this same volume (assuming hexanol was present as 0.004% v/v and not at a lower level in which case a larger amount of Tea Tree Oil would be required) is 2554.25g (0.10217/0.00004). It should also be noted that even if the amount of hexanol is reduced to lower levels for which the inventors also saw an effect upon CFTRs, namely 0.1mM this would require 0.010217g of hexanol for it which would still be necessary to administer 255.425g of Tea Tree Oil.

These calculations are crude but clearly show that there is no way that one of ordinary skill in the art starting with Vail and Swords could have ever ended up with the method according to claim 9 without inundating the lungs of the patient with large quantities of the pungent/irritant/caustic Tea Tree Oil.

The Examiner further contends that the skilled man starting from Vail would in any event realise that the other components of Tea Tree Oil were not having the desired effect and that it was the trace amount of hexanol which should be instead administered in a purified form at the same trace level. However, there is no support for this assertion in the teachings of Vail and Sword.

In fact, it is not clear why one of ordinary skill in the art upon reading the teachings of Vail and Sword could possibly reach such a conclusion or would predict that the teachings of Vail and Sword could be combined as contemplated by the Examiner to arrive at the claimed invention.

Starting from Vail, which relates to methods and apparatus to treat/prevent opportunistic infections in the respiratory tract, assuming the skilled man decided to test this technique in a cystic fibrosis sufferer as pointed out above the quantity of Tea Tree Oil it would have been necessary to administer to a patient to have an effect according to the present invention, would have been impossible to administer. One of ordinary skill in the art would therefore not have seen an effect upon the CFTRs due to the hexanol present according to Swords in the Tea Tree Oil. Any positive effect the skilled man did see in the lungs of a cystic fibrosis sufferer would if

the skilled man approached this situation logically, be considered by the skilled man to be likely due to the more prevalent components of Tea Tree Oil such as 1-Terpinen-4-ol, 1, 8-Cineole or □Terpinene.

The fact that the examiner has stated that the skilled man would choose to isolate hexanol from all the other 48 (according to Swords') components of Tea Tree Oil, shows that this obviousness objection is based upon an *ex post facto* analysis of the prior art with the examiners foreknowledge of the present invention allowing them to state that the skilled man would decide based upon a combination of Vail and Swords to discard all of the other components of Tea Tree Oil leaving them with a trace/unquantified solution of hexanol, which in turn could be used to perform a method to activate the CFTRs of a patient within the scope of claim 9, but not described or suggested by either of these prior art documents.

Finally on the subject of the composition of Tea Tree Oil, the Applicant respectfully disagrees with the Examiner's estimation of the quantity of hexanol in Tea Tree Oil, as the Examiner admits combined gas-chromatography/mass spectrometry does not provide an accurate quantitative estimate of the components found in a sample. The Examiner's estimate of hexanol being 10% as abundant as □-Cubebene based upon the relative sizes of their peaks can not be used to reject the claimed invention as there is no certainty that this estimate is correct and in particular the level of hexanol could be 0.0004% or 0.000004% or indeed the detection of hexanol could be a contaminant. Assuming hexanol is present in Tea Tree Oil for the sake of argument, but that it is present at less than the Examiner's estimated concentration then as pointed out above, this would require Tea Tree Oil to be administered at impossible levels so as to achieve a suitable concentration of hexanol in the vicinity of the defective CFTRs

It should be also noted that although Swords states that Tea Tree Oil contains hexanol, other sources do not. For instance the International Standard for Tea Tree Oil ISO 4730 (2004) states that this Oil comprises the following components at the indicated concentrations:

Component	Concentration [%] v/v
terpinen-4-ol	30-48
γ-terpinene	10–28
α-terpinene	5–13
1,8-Cineole	0–15
α-terpinolene	1.5–5
α-terpineol	1.5–8
α-pinene	1–6
p-cymene	0.5–8

From the above table, it can be seen that Hexanol is not an essential component of Tea Tree Oil. Accordingly, one or ordinary skill in the art starting from Vail and the ISO 4730 would have no basis to eliminate all the essential components of Tea Tree Oil so as to end up with a solution of hexanol for use in a method according to claim 9. For this additional reason, the rejection based on the combination of Vail and Swords should be withdrawn.

In view of the foregoing amendments and remarks, it is respectfully submitted that the rejections under 35 U.S.C. § 102 and 103 have been overcome and that the pending claims are in condition for allowance.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

/Timothy J. Balts/

Timothy J. Balts
Registration No. 51,429

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Charlotte Office (704) 444-1000
Fax Charlotte Office (704) 444-1111
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